```
           1        10        20        30        40        50        60        70        80        90       100
           |--------+---------+---------+---------+---------+---------+---------+---------+---------+---------|
p38        MSQERPTFYRQELNKTIWEVPERYQNLSPVGSGAYGSVCAAFDTKTGHRVAVKKLSRPFQSIIHAKRTYRELRLLKHMKHENVIGLLDVFTPARSLEEFN
ikk         MSWSPSLPTQTCGA--WEMKER------LGTGGFGNVIRWHNQVTGEQIAIKQCRQEL-SPKNRDRWCLEIQIMRRLNHPNVVAARDVPEGMQNLAPND
Consensus  .nqerPslprQecna..WEmkER......lGsGa%GnVcaah#qkTGer!A!Kqcrrel.SiinadRtcrEiri$rr$nHeNV!aarDVfegarnLaen#

           101     110       120       130       140       150       160       170       180       190       200
           |--------+---------+---------+---------+---------+---------+---------+---------+---------+---------|
p38        -DVYLVTHLMGADL----NNIVKCQKLTDDHVQFLIYQILRGLKYIHSADIIHRDLKPSNLAVNEDCEL---KILDFGLARHTDDEM--TGYVATRWYRA
ikk        LPLLAMEYCQGGDLRRYLNQFENCCGLREGAILTLLSDIASALRYLHENRIIHRDLKPENIVLQQGEKRLIHKIIDLGYAKELDQGSLCTSFVGTLQYLA
Consensus  .dllamehcqGaDL....N#ienCcgLr#da!qfLis#IaraLrYiHearIIHRDLKPeNial##dcer...KIiDlGlArelD#em..TgXVaTrqYrA

           201     210       220       230       240       250       260       270       280       290       300
           |--------+---------+---------+---------+---------+---------+---------+---------+---------+---------|
p38        PEIMLNWMHYNQTVDIWSVGCIMAELLTG-RTLFPGTDHID-----QLKLILRLVGTPGAELLKKISSESA-RNYIQSLAQMPKMNFANVFIGANPLAVD
ikk        PEL-LEQQKYTVTVDYWSFGTLAFECITGFRPFLPNWQPVQWHSKVRQKSEVDIVVSEDLNGTVKFSSSSPFPNNLNSVLAERLEKWLQLMLTWQPRQRG
Consensus  PEi.L#qqhYnqTVDiWSfGciaaEciTG.RpllPnt#h!#.....rqKlelriVgseda#glkKiSSeSa.rNni#Slaaerlenfa#lmiga#Prard

           301     310       320       330       340       350       360       370       380       390
           |--------+---------+---------+---------+---------+---------+---------+---------+---------|
p38        LLEK------MLVLDSDKRITAAQAL--AHAYFAQYHDPDDEPVADPYDQSFESRDLLIDEWKSLTYDEVISFVPPPLDQEEMES
ikk        VDPQYGPNGCFRALDDILNLKLVHILNMVTGTIHTYPVMEDESLQSLKTRIREDTGILETDQELLQEAGLVLLPDKPATQCISDSKTNEG
Consensus  ldeq......mraLDddlrikaaqaL..ahatiaqYhdn#DEpladlkdrirEdrdiLed#qelLqeaeL!llpdkPadQcen#S.....
```

Fig. 1(a)

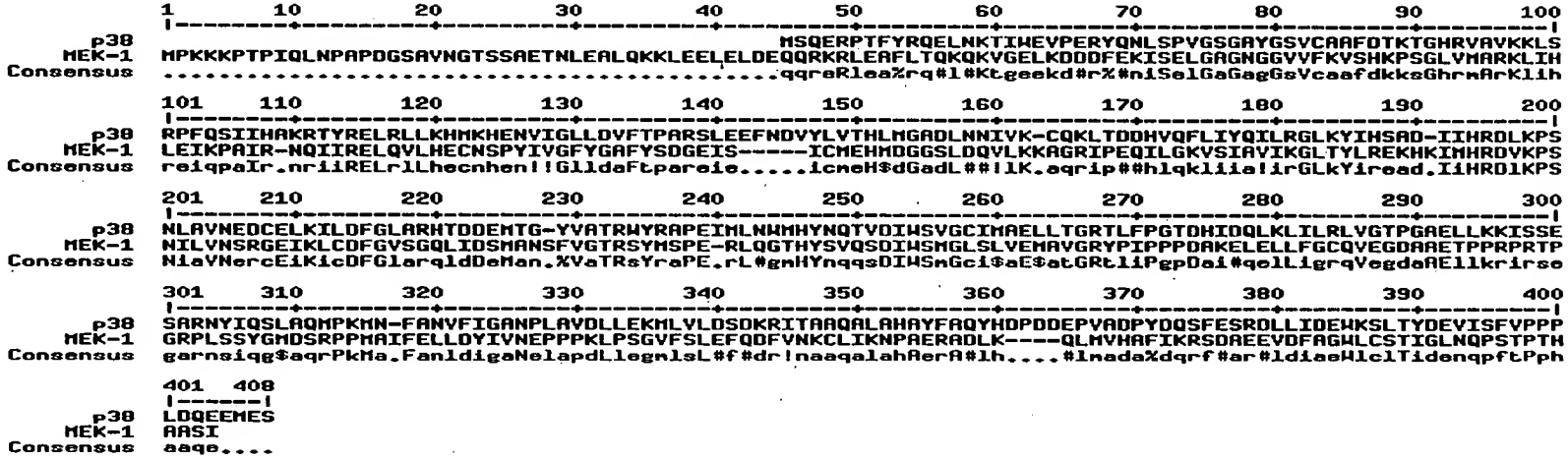

Fig. 1(b)

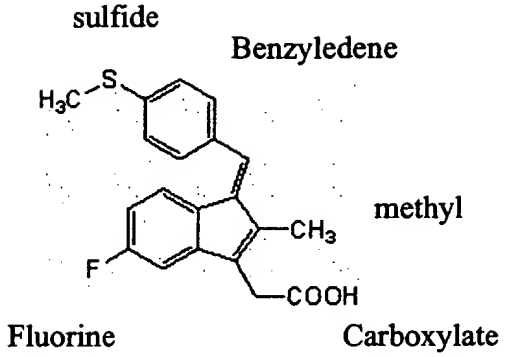
sulfide
Benzyledene
H_3C
S
methyl
CH_3
F
COOH
Fluorine
Carboxylate

Fig. 2(a)

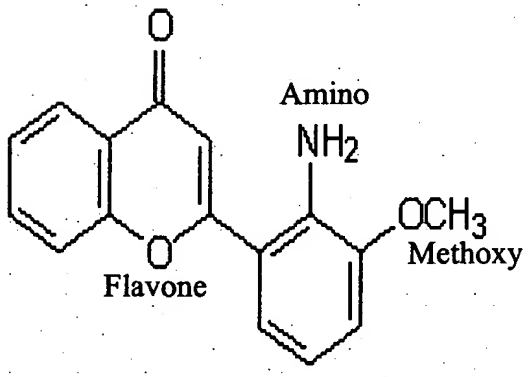
O
Amino
NH_2
OCH_3
Methoxy
O
Flavone

Fig. 2(b)

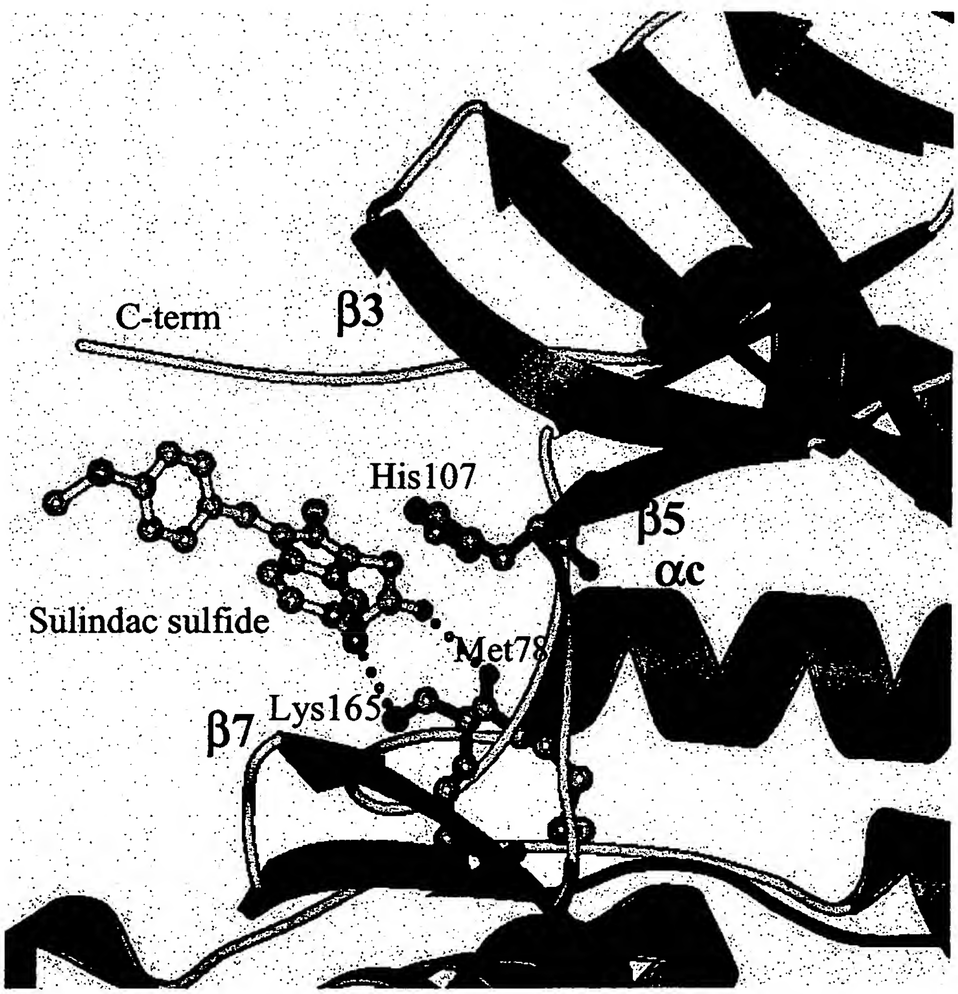

Fig. 3(a)

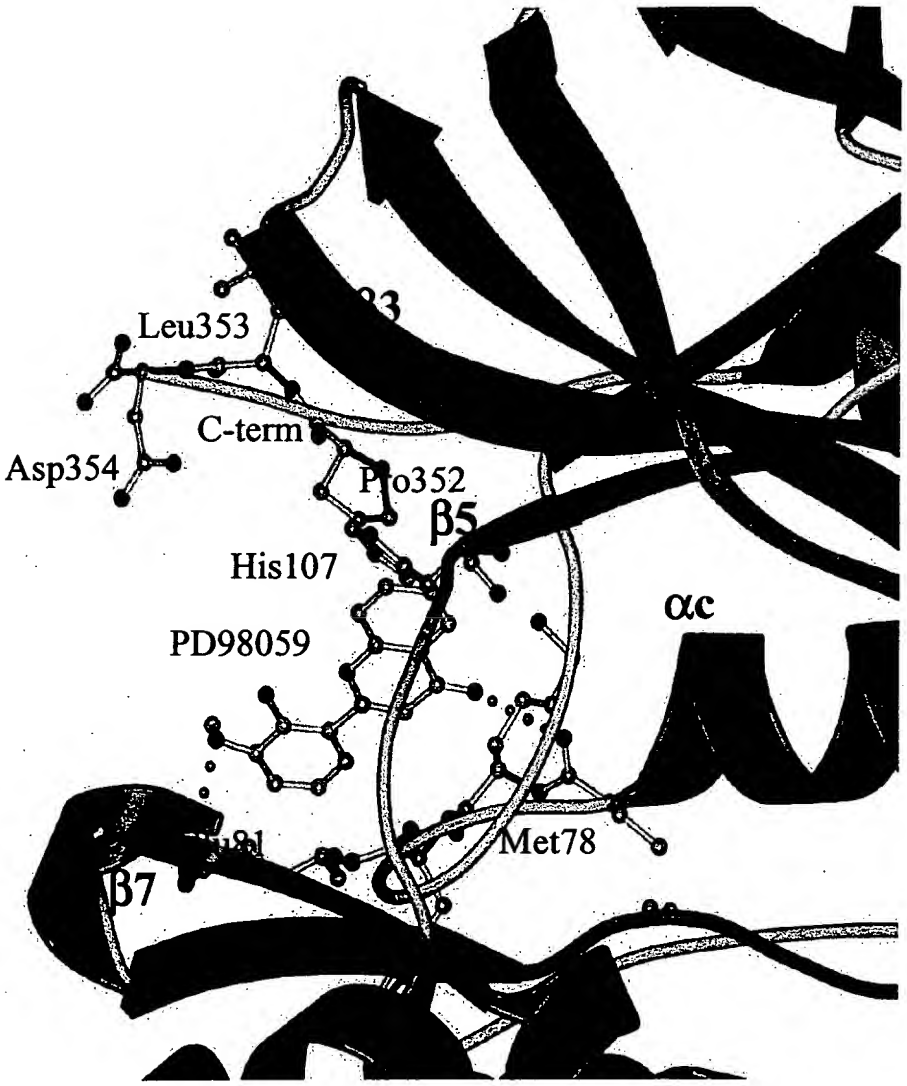

Fig. 3(b)

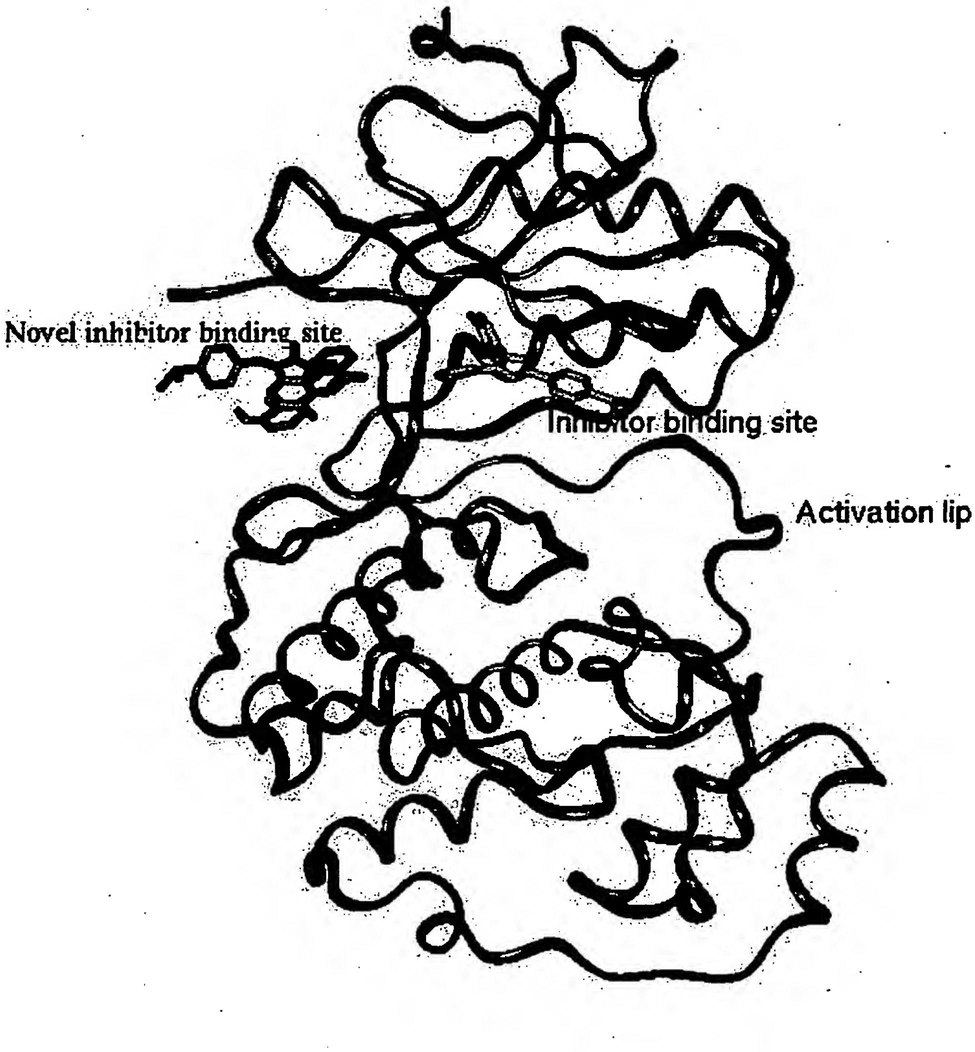

Fig. 4

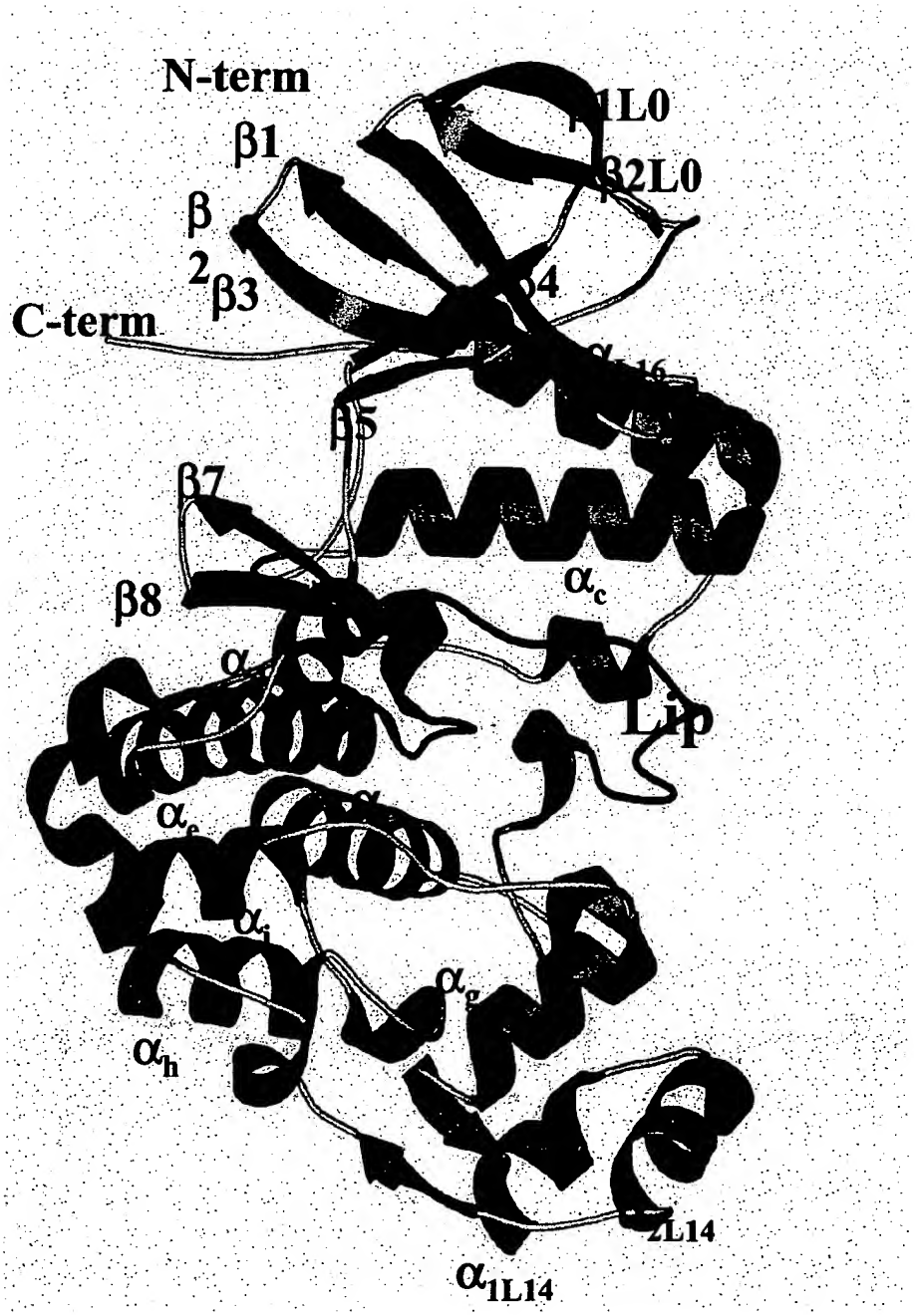
N-term
β1
β2L0
β
2
β3
C-term
β5
β7
β8
α_c
Lip
α_e
α_h
α_{1L14}

Fig. 5

Fig. 6

Linker 2

```
P38    25  Q N L S - - - - - - P V G S G A Y G S V C - - - - - - - A A F
IKK    21  - - - - - - - - - - - L G T G G F G N V I - - - - - - - R W H
MEK1   69  E K I S - - - - - - E L G A G N G G V V F - - - - - - - K V S
JNK3   27  Q N L K - - - - - - P I G S G A Q G I V C - - - - - - - A A Y
GSK3   52  Q E V S Y T D T K V I G N G S F G V V Y - - - - - - - Q A K
Akt   153  D Y L K - - - - - - L L G K G T F G K V I - - - - - - - L V R
NIK   446  R D L T - - - - - - E N V N G M A M N L T T Q V R E I A K V
```

Helix C

```
P38    63  I H A K R T Y R E L - - - - - - - - - - R L L K H
IKK    53  K N R D R W C L E I - - - - - - - - - - Q I M R R
MEK1  107  I R - N Q I I R E L - - - - - - - - - - Q V L H E
JNK3   65  T H A K R A Y R E L - - - - - - - - - - V L M K C
GSK3   91  - - K R F K N R E L - - - - - - - - - - Q I M R K
Akt   192  D E V A H T V T E S - - - - - - - - - - R V L Q N
NIK   491  L D L K N T I N T M V D R L G T F A F E V S K V
```

Linker 5

```
P38    78  M K H E N V I G
IKK    68  L N H P N V V A
MEK1  121  C N S P Y I V G
JNK3   80  V N H K N I I S
GSK3  104  L D H C N I V R
Akt   207  T R H P F L T A
NIK   515  A R E V G T D G
```

Crossover

```
P38   100  N - D V Y L V T H L M G A D L - - - - N - N
IKK    90  D L P L L A M E Y C Q G G D L R R Y L N - Q
MEK1  142  - - - - I C M E H M D G G S L - - - - D - Q
JNK3  102  Q - D V Y L V M E L M D A N L - - - - C - Q
GSK3  119  V - Y L N L V L D Y V P E T V - - - - Y - R
Akt   226  - - - C F V M E Y A N G G D L - - - - F F H
NIK   538  K - D L T E N V N T M A S N L - - - - T - S
```

C-Terminus

```
P38   345  V I S F V P P P L D Q E
IKK   359  L V L L P D K P A T Q C
MEK1  385  N Q P S T P T H A A S I
JNK3  363  V M N S E - - - - - - -
GSK3  374  A T I L I P P H A R I Q
Akt   464  L D Q R T H F P Q F S Y
NIK   788  V F N A L K T L A V K E
```

Fig. 7